

We claim:

1. A method for contrast-enhanced diagnostic imaging of a specific tissue or tissue component that is undergoing or that has undergone interventional therapy, comprising the steps of:

(a) administering to a patient a contrast agent capable of binding to the targeted tissue or tissue component and having a specific affinity for said tissue or tissue component, wherein the contrast agent comprises an image-enhancing moiety (IEM) and a state-dependent tissue binding moiety (SDTBM);

(b) subjecting the patient to one of MRI, ultraviolet light, visible light or infrared light imaging; and

(c) monitoring an imaging signal characteristic of the contrast agent to determine whether the interventional therapy is complete.

2. The method of claim 1, wherein the IEM is selected from the group consisting of organic molecules, metal ions, salts and chelates, particles, clusters, iron particles, labeled peptides, proteins, polymers, liposomes, organic dyes and inorganic dyes.

3. The method of claim 1, wherein the IEM comprises a physiologically compatible chelate comprising at least one cyclic or acyclic organic chelating agent complexed to one or more metal ions with atomic numbers 13, 21-34, 39-42, 44-50 or 57-83.

4. The method of claim 3, wherein the metal ion is a paramagnetic metal ion with atomic numbers 21-29, 42, 44 or 57-83.

5. The method of claim 4, wherein the paramagnetic metal ion is selected from the group consisting of Gd(III), Fe(III), Mn(II), Mn(III), Cr(III), Cu(II), Dy(III), Tb(III), Ho(III), Er(III) and Eu(III).

6. The method of claim 5, wherein the metal ion is Gd(III).

7. The method of claim 5, wherein the chelating agent is selected from the group consisting of DTPA, DOTA, DTPA-BMA and HP-DO3A.

8. The method of claim 1, wherein the IEM comprises a luminescent metal complex.

9. The method of claim 1, wherein the IEM comprises an iron particle or metal chelate of Dy, Gd, or Ho.

10. The method of claim 1, wherein the SDTBM is selected from the group consisting of small-molecules and biomolecules.

11. The method of claim 10, wherein the SDTBM comprises a small-molecule comprising at least one aliphatic, alkoxy, alkylthio, alkylcarbonyl, alkylcarbonyloxy, aryl or heterocyclic group with 1 to 60 carbon atoms and, optionally, one or more nitrogen, oxygen, sulfur, halogen, aliphatic amide, ester sulfonamide, acyl, sulfonate, phosphate, hydroxyl or organometallic substituents.

12. The method of claim 11, wherein the SDTBM comprises at least one aryl ring.

13. The method of claim 11, wherein the SDTBM comprises at least two aryl rings.

14. The method of claim 10, wherein the SDTBM comprises a biomolecule comprising a peptide containing hydrophobic amino acid residues and/or substituents with or without hydrophobic or hydrophilic termination groups.

15. The method of claim 1, wherein the contrast agent exhibits a state-dependent binding affinity for a tissue or tissue component in plasma, interstitial space, synovial fluid, cerebral spinal fluid, inflammatory fluid, abscess fluid or intracellular space.

16. The method of claim 1, wherein the contrast agent exhibits a state-dependent binding affinity for a protein selected from the group consisting of human serum albumin, fatty acid binding protein, glutathione-S-transferase and lipoproteins.

17. The method of claim 1, wherein the contrast agent further comprises a blood half-life extending moiety (BHEM) which possesses one or more full or partial negative charges in aqueous solution at physiological pH wherein the negative charge cannot be partially or fully neutralized by covalent or coordinate covalent bonding to the IEM.

18. The method of claim 17, wherein the contrast agent exhibits a state-dependent binding affinity for human serum albumin.

19. The method of claim 18, wherein at least 10% of the agent binds to human serum albumin in its native state.

20. The method of claim 18, wherein at least 50% of the agent binds to human serum albumin in its native state.

21. The method of claim 18, wherein at least 80% of the agent binds to human serum albumin in its native state.

22. The method of claim 18, wherein at least 95% of the agent binds to human serum albumin in its native state.

23. The method of claim 18, wherein the contrast agent exhibits a binding affinity for human serum albumin in its denatured state which is less than about 80% of the contrast agent's binding affinity for the human serum albumin in its native state.

24. The method of claim 18, wherein the contrast agent exhibits a binding affinity for human serum albumin in its denatured state which is less than about 50% of the contrast agent's binding affinity for the human serum albumin in its native state.

25. The method of claim 18, wherein the contrast agent exhibits a binding affinity for human serum albumin in its denatured state which is less than about 20% of the contrast agent's binding affinity for the human serum albumin in its native state.

26. The method of claim 18, wherein the contrast agent exhibits a binding affinity for human serum albumin in its denatured state which is less than about 10% of the contrast agent's binding affinity for the human serum albumin in its native state.

27. The method of claims 1 or 18, wherein the contrast agent exhibits an  $R_1$  relaxivity when bound to the tissue or tissue component in its denatured state which is less than about 80% of the  $R_1$  relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

28. The method of claims 1 or 18, wherein the contrast agent exhibits an  $R_1$  relaxivity when bound to the tissue or tissue component in its denatured state which is less than about 50% of the  $R_1$  relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

29. The method of claims 1 or 18, wherein the contrast agent exhibits an  $R_1$  relaxivity when bound to the tissue or tissue component in its denatured state which is less than about 20% of the  $R_1$  relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

30. The method of claims 1 or 18, wherein the contrast agent exhibits an  $R_1$  relaxivity when bound to the tissue or tissue component in its denatured state which is less than about 10% of the  $R_1$  relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

31. The method of claims 1 or 18, wherein the contrast agent exhibits an  $R_1$  relaxivity when the interventional therapy is complete and the targeted tissue or tissue component is returned to physiological conditions which is less than about 80% of the  $R_1$  relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

32. The method of claims 1 or 18, wherein the contrast agent exhibits an  $R_1$  relaxivity when the interventional therapy is complete and the targeted tissue or tissue component is returned to physiological conditions which is less than about 50% of the  $R_1$  relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

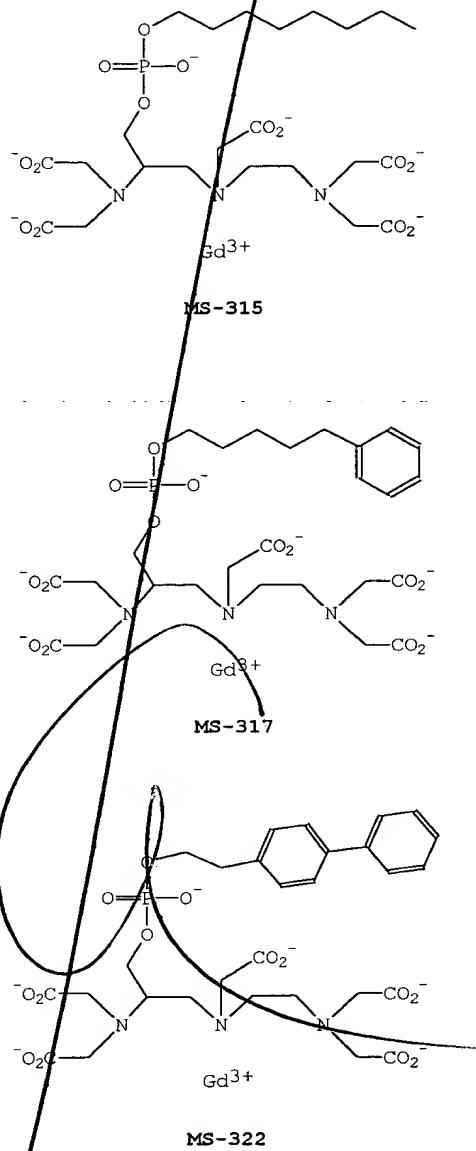
33. The method of claims 1 or 18, wherein the contrast agent exhibits an  $R_1$  relaxivity when the interventional therapy is complete and the targeted tissue or tissue component is returned to physiological conditions which is less than about 20% of the  $R_1$  relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

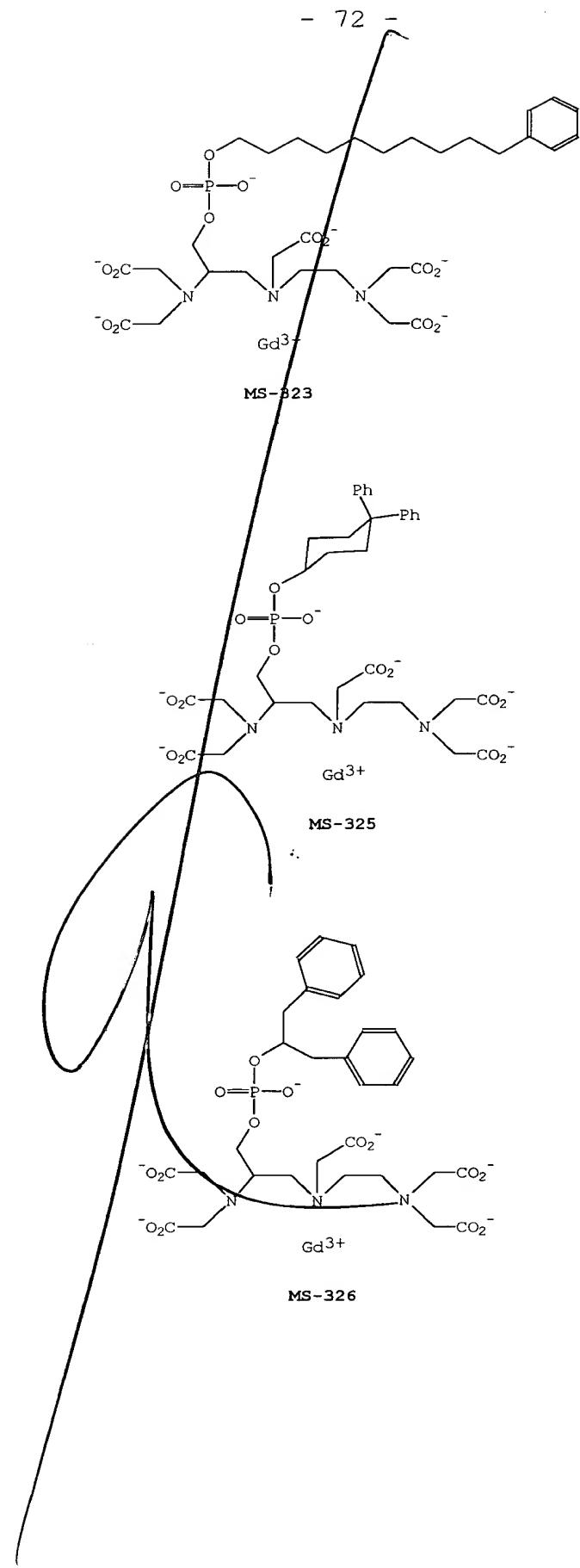
34. The method of claims 1 or 18, wherein the contrast agent exhibits an  $R_1$  relaxivity when the interventional therapy is complete and the targeted tissue or tissue component is returned to physiological conditions which is less than about 10% of the  $R_1$  relaxivity of the contrast agent when bound to the tissue or tissue component in its native state.

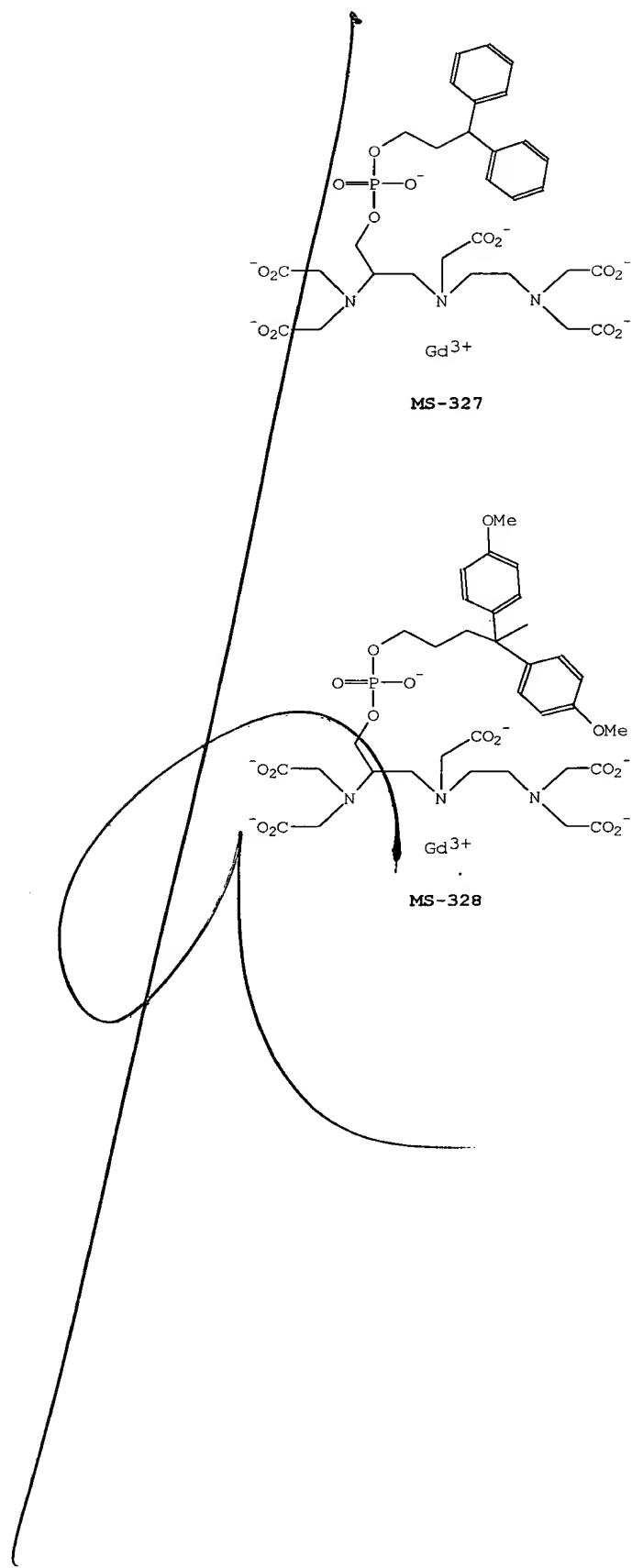
35. A method for contrast-enhanced diagnostic imaging of a specific tissue or tissue component that is

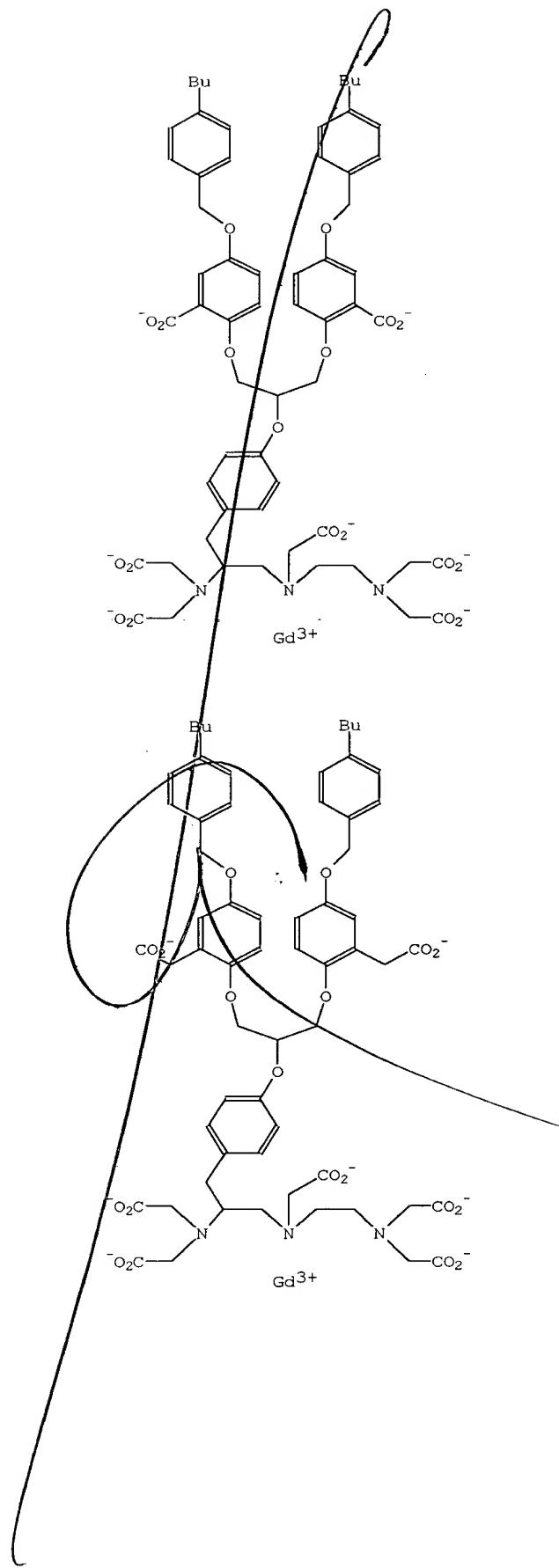
undergoing or that has undergone interventional therapy, comprising the steps of:

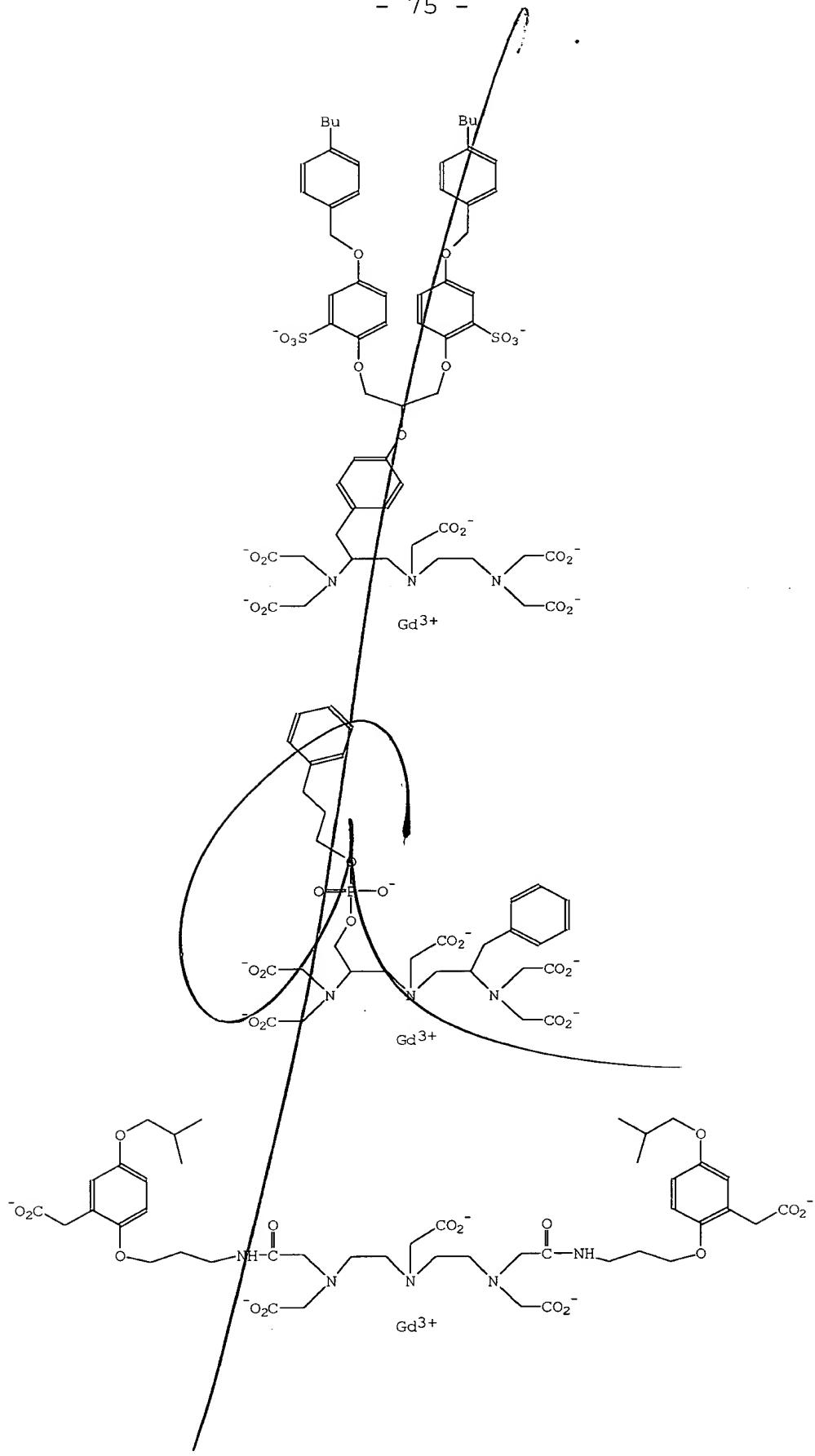
(a) administering to a patient a contrast agent having one of the following formulas:

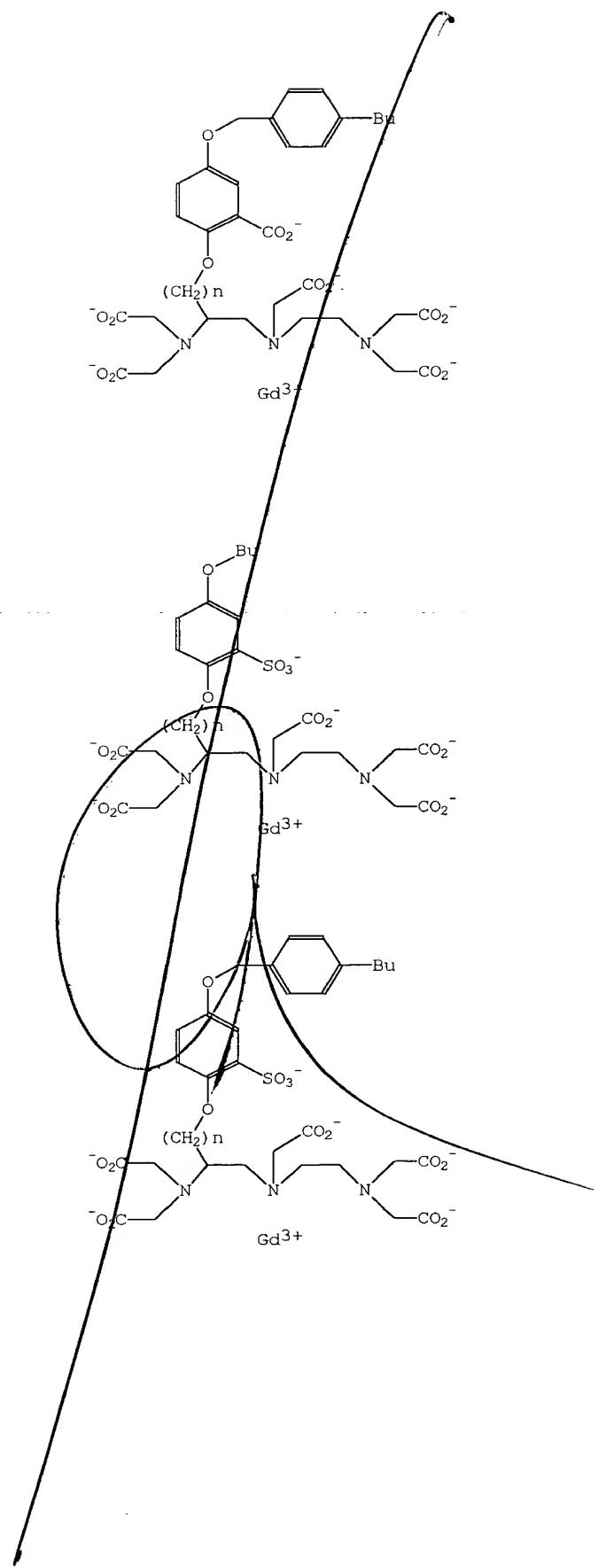


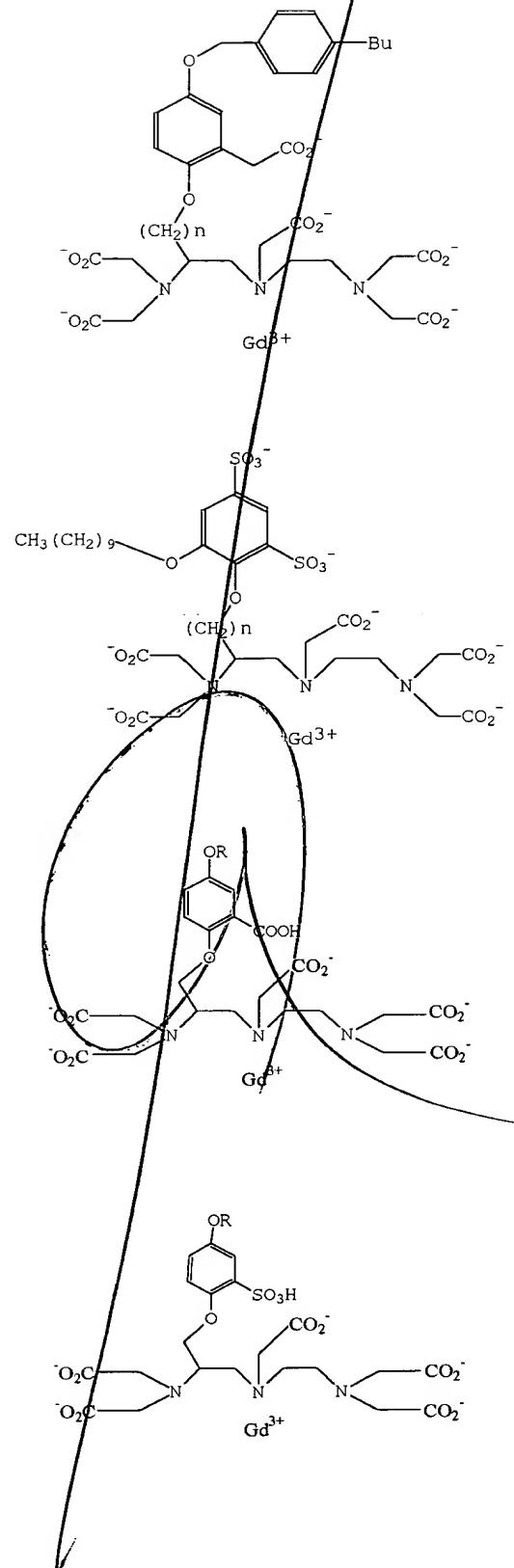












wherein n can be 1 to 4, and R comprises an aliphatic group and/or at least 1 aryl ring;

(b) subjecting the patient to one of MRI, ultraviolet light, visible light or infrared light imaging; and

(c) monitoring an imaging signal characteristic of the contrast agent to determine whether the interventional therapy is complete.

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